Food Chemistry 250 (2018) 268–275

Contents lists available at ScienceDirect

Food Chemistry

journal homepage: www.elsevier.com/locate/foodchem

Profiling wines in China for the biogenic amines: A nationwide survey and pharmacokinetic fate modelling

Runhui Ke[a,b,1], Zongsu Wei[c,1], Christian Bogdal[d], Recep Kaya Göktaş[e], Ruiyang Xiao[a,*]

[a] Institute of Environmental Engineering, School of Metallurgy and Environment, Central South University, Changsha 410083, China
[b] China National Research Institute of Food and Fermentation Industries, Beijing 100015, China
[c] Laboratory for the Chemistry of Construction Materials (LC^2), Department of Civil and Environmental Engineering, University of California, Los Angeles, CA 90095, USA
[d] Institute for Chemical and Bioengineering, ETH Zurich, Vladimir-Prelog-Weg 1, CH-8093 Zürich, Switzerland
[e] Department of Environmental Engineering, Kocaeli University, Umuttepe Yerleşkesi, 41380 İzmit, Kocaeli, Turkey

ARTICLE INFO

Keywords:
Biogenic amines
Red wine
Nationwide survey
PBPK

ABSTRACT

Biogenic amines (BAs), a class of nitrogenous compounds that are frequently detected in wine, pose adverse effects to humans. However, with the largest red wine consumption in the world, little is known about national profiles correlating BAs in wines to toxicological/health risks in China. In this study, we conducted a nationwide survey of commercially available wines for the occurrence of BAs. Our sampling campaign covered > 90% of wine brands (n = 456) in China in a three year span (2014–2016). The target BAs included tryptamine, phenylethylamine, putrescine, cadaverine, histamine, tyramine, spermidine and spermine. In order to quantitatively characterize the potential risk and/or support regulatory decision-making, chronic and acute BA exposure scenarios were developed and simulated with a physiologically based pharmacokinetic model. The model described the fate and transport of BAs within human body using physical descriptions of relevant processes. These results provided baseline data that are needed for the risk assessment of dietary uptake of BAs and evaluating winemaking processes by food safety authorities.

1. Introduction

Biogenic amines (BAs) are low molecular weight nitrogenous compounds that are frequently detected in fermented food and wine (Ancin-Azpilicueta, Gonzalez-Marco, & Jimenez-Moreno, 2008; Blackwell & Mabbit, 1965). They originate as a result of complex processes during winemaking. Although putrescine was reported to be produced in grape due to low potassium concentration in soils (Landete, Ferrer, Polo, & Pardo, 2005), most BAs were formed via decarboxylation of amino acids (Anli & Bayram, 2009). Amino acid content was attributed to be the main reason for BA formation in the winemaking process, where malolactic fermentation was the main process to produce histamine and tyramine (Costantini, Vaudano, Del Prete, Danei, & Garcia-Moruno, 2009; Marcobal, Martin-Alvarez, Polo, Munoz, & Moreno-Arribas, 2006). In addition, the BA formation was evidently related to the wine quality (Costantini et al., 2009; Garcia-Villar, Hernandez-Cassou, & Saurina, 2007), thus the detection of BA is used as an indicator for hygiene conditions of industrial manufacture of red wines (Beneduce et al., 2010).

Although BA are indispensable components of living cells and important in the regulation of several natural physiological processes, the intake of large amounts of BA can pose adverse physiological effects to consumers including headaches, heart palpitation, hyper/hypotension and respiratory distress (Littlewood et al., 1988; Shalaby, 1996). BAs in wines potentially exacerbate the side effects due to the synergistic interaction with alcohol, especially to susceptible humans (Heberger, Csomos, & Simon-Sarkadi, 2003; Konakovsky et al., 2011). Therefore, upper limits from 2 to 10 mg L^{-1} of amines (such as histamine) are suggested for red wine industry in European countries such as Germany, Belgium, France, and Switzerland (Landete et al., 2005). The content of BAs for red wines in Chinese market may be regulated in the near future following the suggested limits of the European market. To date, China is the leading red wine consumer with 1.86 billion domestic and imported bottles sold in 2013 (Willsher, 2014). With anticipation of steady growth for red wine industry in next decade, such vast amount of consumption of red wines raises increasing concern of adverse health effects of BAs to the Chinese public. Yet, national profiles correlating BAs to toxicological risks have not been established. There are limited survey for the BA contents in Chinese red wines with data collected from either a very small size sampling or limited production regions (Li,

* Corresponding author.
E-mail address: xiao.53@csu.edu.cn (R. Xiao).
[1] Both Runhui Ke and Zongsu Wei contributed equally to this study.

https://doi.org/10.1016/j.foodchem.2018.01.040
Received 18 September 2017; Received in revised form 10 December 2017; Accepted 3 January 2018
Available online 04 January 2018

Wu, Zhang, Zhao, & Xue, 2007). A large data set from various production sites and vintage years is necessary to establish BA profiles as red wine fingerprint. Such quantitative analysis of BA levels is essential to evaluate the status of quality control, and provide scientific basis for safety control in winemaking process (Bisson, Waterhouse, Ebeler, Walker, & Lapsley, 2002).

In this study, we sampled most of the commercially available wines in China, covering > 90% of domestic wine brands in the market. In a three year span (2014–2016), a total of 456 wine samples were collected to monitor BA levels from different geographical origins of China. The target BAs included tryptamine (TRY), phenylethylamine (PHE), putrescine (PUT), cadaverine (CAD), histamine (HIS), tyramine (TYR), spermidine (SPD) and spermine (SPM). These amines were selected due to their common presence in wine and potential toxicological/health impacts to humans. It is worthy of mentioning that contents of PUT could be used as an indicator to evaluate the potential unsanitary production conditions during wine manufacturing. But there is no established maximum-allowable limits on the BAs content for alcoholic beverages in China. Further, a physiologically based pharmacokinetic (PBPK) model with chronic and acute BAs exposure scenarios was developed and analyzed with the purpose of quantitative characterization of potential risk on individuals and/or regulatory decision-making (Nadal, Fabrega, Schuhmacher, & Domingo, 2013). To the best of our knowledge, this is the first study at the national level to assess and link the BA contents to potential health risks for the largest group of wine consumers.

2. Methods

2.1. Experimental method

2.1.1. Standards and reagents

Target compounds, namely TRY, PHE, PUT, CAD, HIS, TYR, SPD, and SPM, were purchased from Sigma-Aldrich and Dr. Ehrenstorfer GmbH without further purification. Internal standard 1,7-diaminoheptane was purchased from TCI Japan. Derivatization agent dansyl chloride (DCl) was obtained from CNW Technologies GmbH, Germany. Major solvents, such as methanol, acetone, and ethyl acetate were obtained from J.T. Baker (USA). Ultrapure water (18.2 MΩ·cm, 25 °C) was obtained with a Milli-Q Reference System (Millipore, USA). Other common reagents, such as hydrochloric acid, sodium chloride, sodium hydroxide, sodium bicarbonate, *n*-butyl alcohol, chloroform, and diethyl ether were from the Beijing Chemical Works, and were of analytical or higher grade.

2.1.2. Sample collection and preparation

A total of 456 commercial wines produced in different regions from various grape species were analyzed in this work. According to the labeling information on the bottles, 341 were dry red wine, 57 semi-dry red wine, 28 semi-sweet/sweet wine, 19 dry white wine, 8 semi-dry white wine, and 3 rose wine.

BAs stock standard solutions (1 mg mL^{-1}) were prepared by dilution with 0.1 M HCl and stored at 4 ± 1 °C. The working standard solution was prepared daily for freshness. The derivatization agent solution was prepared by dissolving 100 mg of DCl in 10 mL of acetone, and was also stored at 4 ± 1 °C. The extraction and derivatization procedures of our method were conducted on the basis of GB/T 5009.208 (National Standard of the People's Republic of China, 2008) and the classical BA analytical method by Dugo, Vilasi, La Torre, and Pellicano (2006). The derivatization reactions of these methods were the same as the method by Preti, Antonelli, Bernacchia, and Vinci (2015). In addition, a core–shell particle UHPLC column (Halo C_{18} column, 2.1 mm × 50 mm, 2.7 μm) used in our method is similar to the column used by Preti et al. (2015), For improving the detection sensitivity, a time-consuming concentration step of extracting BAs from the wine samples with *n*-butanol–chloroform (1:1, v/v) was added before derivatization. Briefly, a 10-ml aliquot of samples was accurately transferred into a centrifuge tube, and 400 μL of 1, 7-diaminoheptane (100 μg mL^{-1}) was added. The samples were saturated using sodium chloride, and then pH was adjusted to 12 using 0.2 M sodium hydroxide. The samples were extracted with 5 mL *n*-butanol–chloroform (1:1, v/v) solution in the test tube. The tube was vortexed for 5 min and then centrifuged for 10 min at 2000 rpm. A 3-mL aliquot of the extract was transferred into a 10 mL test tube with stopper. 0.2 mL 1 M hydrochloric acid was added to the organic extract and then evaporated to dryness under a stream of nitrogen with heating at 40 °C. The residue was dissolved in 0.5 mL of 0.1 M hydrochloric acid for derivatization. 1.5 mL of saturated $NaHCO_3$ and 1.0 mL of DCl solution (10 mg mL^{-1} in acetone) were added into the test tube. The mixture was vortex mixed for 30 s and then incubated for 60 min at 60 °C. After the reaction, the derivatized solution was cooled and extracted 3 times with diethyl ether (2 × 3 mL) and ethyl acetate (3 mL). The organic phases were collected and evaporated to dryness. Then, the residue of the dansyl derivatives was dissolved in 1.0 mL methanol-water (8/2, v/v) solution. This solution was filtered through a 13 mm PVDF syringe filter (0.45 μm pore size) prior to HPLC analysis.

2.1.3. Instrumental analysis

The HPLC system (Shimadzu, Japan), equipped with an auto-sampler SIL-20A XR, CTO-20AC Prominence Column oven, and an ultraviolet detector (SPD-20A Prominence UV/Vis detector) was used for the amines measurements. Separation was performed on a Halo C_{18} column (2.1 mm × 50 mm, 2.7 μm) from Advanced Materials Technology, Inc. (Wilmington, USA) at 40 °C. The binary mobile phase was composed of methanol (A) and water (B). The following gradient program was used: 0–1.5 min 55–65% A, 1.5–3 min 65–70% A, 3–5 min 70–70% A (isocratic step), 5–7 min 70–90% A, 7–8 min 90–100% A, 8–8.5 min 100–100% A (isocratic step), and 8.5–9 min 100–55% A with the flow rate of 0.3 mL min^{-1}, achieving a complete separation in < 11 min. UV detection was set at 254 nm. A series of diluted standard solutions contained eight BAs and 1,7-diaminoheptane was prepared from the standard stock solutions and used to obtain the standard curves for each BA.

2.1.4. Quality assurance

The instruments were calibrated daily with the standards and the relative percent difference between the five-point calibrations. In general, the calibrations should be < 20% for all of target analytes to verify the accuracy. If a calibration standard was > 20% of the existing calibration, the standard curve should be rebuilt. Method blanks (solvents), spiked blanks (standards spiked into solvent), and sample duplicates were routinely checked. No target chemicals were found in the process blanks. The spiked blanks were routinely conducted to check the recovery for each batch. The recovery rates for the eight amines were detected within 70–120%. In addition, internal standard were added to all the samples to monitor matrix effects. The recovery tests were carried out by spiking the samples with a known amount of the analyte (*i.e.,* 1, 2, and 10 mg L^{-1}) in the wine samples. The average recoveries of eight amines in three matrix spikes varied from 82.8% to 109% (Table S1). No analytical results were corrected by the recovery rate. The limit of detection (LOD) was estimated for a signal-to-noise ratio of > 3 from the chromatograms of samples spiked at the lowest concentration validated. The LODs for eight amines are also tabulated in Table S1. Limit of quantitation for all the amines were set at 0.1 mg L^{-1}.

2.2. PBPK modelling

2.2.1. PBPK model

A general physiologically based pharmacokinetic (PBPK) model was used in order to estimate the tissue concentrations of BAs in humans after intake via wine consumption. The PBPK model used has been